1123-187 **Soluble CD40 Ligand in Pulmonary Arterial Hypertension: Possible Pathogenic Role of Interaction Between Platelets and Endothelial Cells**

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Background: Inflammatory processes seem to be involved in the development and progression of pulmonary arterial hypertension (PAH). CD40 ligand (L) may induce various biological responses such as matrix degradation and thrombus formation in several inflammatory disorders. We hypothesized that CD40L also could be involved in the immunopathogenic mechanisms of PAH.
Methods and Results: By comparing soluble (s) CD40L levels in 32 PAH patients and 8 controls, we found several significant differences: 1) Patients with primary pulmonary hypertension (n=13) and secondary PAH (n=11) had increased sCD40L levels comparing controls ($p<0.05$ and $p<0.01$, respectively). 2) In contrast, sCD40L levels were normal in patients with chronic thromboembolic pulmonary hypertension (n=8) and in other PAH patients using warfarin. 3) sCD40L levels were higher in arterial (femoral artery) comparing mixed venous blood (pulmonary artery), suggesting production of CD40L in the pulmonary vasculature. 4) Platelets from patients with PAH showed higher intracellular levels, enhanced spontaneous and thrombin-stimulated release of sCD40L comparing controls ($p<0.01$). Finally, in vitro studies demonstrated that sCD40L induced chemokine expression (i.e. MCP-1 and IL-8) in endothelial cells. Indeed, MCP-1 and IL-8 were elevated and correlated to pulmonary vasculature resistance in PAH ($p<0.01$). Surprisingly, prostacycline enhanced MCP-1 levels in PAH patients in vivo and in CD40L-stimulated HUVEC in vitro, suggesting some unfavorable effects of this medication in PAH.
Conclusion: Raised platelet-derived CD40L levels in PAH patients may (i) reflect enhanced platelet activation and thrombus formation in these patients, and (ii) induce chemokine expression in endothelial cells. These processes could contribute to the the pathogenesis of this disorder.

1123-188 **Role of Amlodipine in Preventing and Reversing Monocrotaline-Induced Pulmonary Arterial Hypertension in Rats**

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Background: Amlodipine has been reported to be beneficial to improve coronary microvascular endothelial function, inhibit proliferation of vascular smooth muscle cells and expression of matrix metalloproteinase-1 in vascular endothelial cells, and exert antioxidant actions. The present study was designed to examine the role of amlodipine in preventing and reversing monocrotaline (MCT)-induced pulmonary arterial hypertension (PAH) in rats. Methods: Rats were injected with 40 mg/kg of MCT subcutaneously and randomized to either 6mg/kg/day of amlodipine in drinking water or placebo for 3 weeks. Animals treated with MCT and survived for 3 weeks were assigned to either amlodipine (6mg/kg/day) or placebo for next 3 weeks. The animals had measurement of cardiac weights and pulmonary arterial pressure, and then underwent histologic and Western blot analyses of the lung tissue after treatment. Results: Amlodipine immediately following MCT injection markedly inhibited PAH (mean pulmonary arterial pressure: 32.0 ± 2.9 mmHg in the placebo group vs 16.4 ± 2.1 mmHg in the amlodipine-treated group, $p < 0.01$) with severe pulmonary vascular remodeling and right-sided heart failure. The survival rate at 3 weeks after treatment was significantly increased in the amlodipine-treated group compared with the placebo group (90 % vs 44 %, $p < 0.05$). eNOS expression in the lung tissue was significantly reduced in the placebo group, but it was markedly improved after 3 weeks of amlodipine ($p < 0.001$). Late treatment with amlodipine did not palliate PAH nor improved survival. Conclusions: Amlodipine immediately after MCT injection inhibited development of PAH and improved survival in rats. These effects were associated with marked upregulation of eNOS in the lung tissue. In contrast, amlodipine failed to reverse established PAH. Thus, this study may provide an insight into therapeutic strategy of amlodipine in PAH.

POSTER SESSION

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Lipids and Prevention

Tuesday, March 09, 2004, 9:00 a.m.-11:00 a.m.
Morial Convention Center, Hall G
Presentation Hour: 9:00 a.m.-10:00 a.m.

1124-189 **Degree of Physical Activity Is Associated With Subclinical Atherosclerosis in Patients Prone to Metabolic Syndrome**

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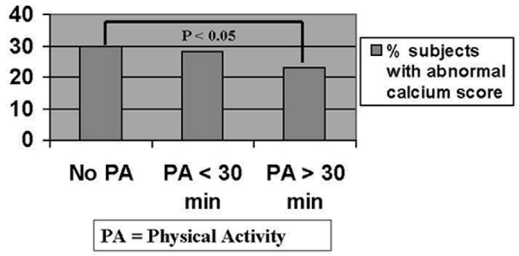
Background: Metabolic syndrome (MS) is a risk factor for the development of subclinical atherosclerosis (SA). SA and lack of physical activity (PA) predict coronary heart disease, however, it is not known whether duration and frequency of PA impacts development of SA in patients prone to develop MS. We assessed the impact of different degrees of PA on SA in patients with MS. **Methods:** We studied 779 patients with MS (patients with overt diabetes were excluded) referred for electron beam tomography. MS was defined as blood pressure > 130/85 mm Hg**,** triglycerides > 150 mg/dl, HDL < 40 mg/dl and body mass index > 30 kg/m^2 (subjects meeting ≥ 2 criteria were included). Patients were divided into 3 groups: 1 (n = 308) = no PA, 2 (n = 189) = PA < 30 minutes ≥ 2 times/week and 3 (n = 282)= PA > 30 minutes ≥ 2-3 times/week. Abnormal coronary artery calcification (ACAC) or significant SA was defined as a calcium score > 75th percentile based on gender and age. **Results:** Patients were 67 % males with a mean age of 54 ± 9 years. ACAC was present in 30 % of Group 1 patients, 28 % of Group 2 patients and 23 % of Group 3 patients (figure). Patients without PA had 23 % higher relative probability of ACAC than patients in the highest PA category ($p < 0.05$), a finding that persisted after correction for gender. Lesser degree of PA did not significantly reduce the prevalence of ACAC. **Conclusion:** Patients who are prone to MS have a higher prevalence of SA in the presence of little or no PA relative to those who engage in PA at least 30 minutes per sessions, 2 times a week.



1124-190 **Inpatient Cardiac Risk Factor Management Program Can Promote Therapeutic Lifestyle Change**

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Background: The STARR (Steps to Achieve Risk Reduction) program is a multi-disciplined inpatient program designed to improve patient knowledge of cardiac risk factors, increase AHA/ACC guideline adherence, and promote lifestyle change. With shorter hospitalizations, it is important to use systematic health delivery strategies for quality care. While clinical goals have been obtained with similar programs, little is published regarding the ability to promote longterm therapeutic lifestyle change (TLC) in the acute setting. The STARR program addresses diet, exercise, weight loss, tobacco, stress, hypertension, lipids, and diabetes.
Methods: STARR utilizes a multi-disciplined approach to educate and manage cardiovascular risk in patients admitted to Emory Hospital. The program uses an algorithm based on clinical trials and AHA/ACC recommendations. Patient education is accomplished with a multidisciplinary team and reinforced with educational booklets, magnets, stickers, and patient contracts. Prior to STARR, a control group of 18 patients underwent phone interview 5 months after discharge and answers recorded on a standardized database. Patients were evaluated separately on their knowledge of risk reduction goals and self-reported compliance with diet and exercise. Post STARR, 30 patients were followed 5 months after discharge to assess STARR's impact on knowledge and behavioral compliance with risk reduction. Mean score differences were compared with unpaired Student's t-test.
Results: Five months after discharge, the STARR patients' knowledge of exercise and diet goals was 56.7% (95%CI 47.2-66.1%) versus 18.2% (95%CI 9.5-26.9%) in controls (p value <0.0001). The STARR patients' exercise and diet compliance was 67% (95%CI 57.5-75.9) versus 43.5% (95% CI 33.2-53.8, p=0.002). In STARR patients, there was a trend toward improvement in stress, weight, blood pressure, diabetic, and lipid goals.
Conclusion: An acute inpatient multi-disciplinary based program can influence knowledge and compliance regarding TLC in diet and exercise. This benefit is sustained at 5 months and follow up will assess if it is maintained. Long term, STARR should lower cardiac morbidity and mortality.

1124-191 **Predictive Risk Factors for Coronary Events in Renal Transplant Patients**

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A number of observational studies have indicated that coronary heart disease is more common among renal transplant recipients than in the general population. However, in renal transplant patients the relation between conventional cardiac risk factors and cardiac events is less clear than in other populations. Renal transplant recipients may also acquire non-traditional risk factors as a consequence of renal transplantation procedures. In the ALERT study, 2102 stable renal transplant recipients (total cholesterol 4.0 – 9.0 mmol/l (received fluvastatin (n=1050) or placebo (n=1052) for a median period of 5.1 years. We analysed the role of traditional and non-traditional risk factors in the placebo arm of the ALERT study (Lancet 2003;361:2024).
Methods. A univariate risk factor analysis to assess the influence of a large set of potential risk factors for a predefined composite endpoint (Cardiac Death or Non-fatal MI) was performed. Subsequently a multivariate model building approach was used to determine